

Principal Researcher	Ryozo Nagai			Number of Researchers	3	
Research Institution · Department · Title	Professor, Graduate School of Medicine, Department of Cardiovascular Medicine, University of Tokyo			Location of Institution	Bunkyo-ku, Tokyo	
Title of Project	Molecular mechanism of organ remodeling: Gene transcription and cell-cell interaction in mesenchymal cells					
Abstract of Research Project	<p>External stress activates local cells of the mesenchymal origin (e.g., fibroblasts and smooth muscle cells) and inflammatory cells. Interactions between these cells promote fibrosis, organ hypertrophy, and structural remodeling. These changes affect the function of organs and result in organ failure including heart failure, renal failure, and liver failure. Thus, elucidation of molecular mechanisms underlying the tissue remodeling would lead to development of novel therapeutic strategies for protection of normal organ function. We have identified a Krppel-like zinc finger transcription factor BTEB2 that is important for atherosclerosis, restenosis after angioplasty, tissue fibrosis, and cardiac hypertrophy. We have also found that the ageing related factor Klotho inhibits tissue remodeling of the cardiovascular system. In this research project, we will study transcriptional regulation and signal transduction that control tissue remodeling. The goals of the project are: 1) elucidation of the transcription factor network involved in inactivation of mesenchymal cells in tissue remodeling; 2) elucidation of signal transduction mechanisms involved in the protective function of the Klotho factor against stress in the cardiovascular system; and 3) development of drugs targeting transcription factors and humoral factors that are important for remodeling.</p>					
References	<p>1) T Shindo, I Manabe, Y Fukushima, K Tobe, K Aizawa, S Miyamoto, K Kawai-Kowase, N Moriyama, Y Imai, H Kawakami, H Nishimatsu, T Suzuki, H Morita, K Maemura, M Sata, M Komukai, H Kagechika, TKadowaki, MKurabayashi, RNagai Krppel-like zinc-finger transcription factor KLF5/BTEB2 is a target for angiotensin II signaling and an essential regulator of cardiovascular remodeling. <i>Nature Med</i> in press</p> <p>2) Watanabe N., Kurabayashi M., Manabe I., Watanabe M., Suzuki T., Yazaki Y. and Nagai R. BTEB2, a Kruppel-like transcription factor, regulates expression of the SMemb/Nonmuscle myosin heavy chain B (SMemb/NMHC-B) gene. <i>Circ Res</i>;85:182-191,1999</p>					
Term of Project	Fiscal years 2002-2006. (5years)					
Budget Allocation (in thousand of yen)	FY2002	FY2003	FY2004	FY2005	FY2006	TOTAL
	18,300	17,200	17,200	17,200	12,900	82,800